

**Title: A trial to evaluate the effect of Vitamin D  
supplementation in patients with Chronic Urticaria**

**Institutional ethics committee approval number: INT/IEC/2017/1314**

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**Principal Investigator:**

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**Co-investigator: Dr. Sendhil Kumaran**, Associate Professor, Department of Dermatology,  
Venereology & Leprology, PGIMER, Chandigarh

# **Title: A trial to evaluate the effect of Vitamin D supplementation in patients with Chronic Urticaria**

## **Summary of proposed research**

Chronic urticaria (CU) is characterized by recurrent, raised, pruritic wheals lasting for more than 6 weeks, for at least 2 or more times per week and may be accompanied by angioedema in 30-60% patients. Lifetime prevalence of CU is approximately 1.8% in general population, <sup>(1)</sup> with a point prevalence rate of 0.6-0.8% in adults <sup>[2]</sup> and affecting females more often than males. <sup>[2,3]</sup> Chronic spontaneous urticaria (CSU) is diagnosed after excluding all causes of physical urticaria and in most cases there is no definite cause. Antihistamines constitute the mainstay of therapy in CSU. Second line drugs include systemic corticosteroids, anti-leukotrienes, hydroxychloroquine, cyclosporine, dapsone and omalizumab.<sup>[4]</sup>

Vitamin D (Vit D), is a fat soluble vitamin having endocrine, paracrine and autocrine functions produced in the skin after ultraviolet radiation exposure or obtained from diet and supplements. Apart from its effect on bone and mineral metabolism, it exerts several immunomodulatory actions in both innate and adaptive immunity via Vit D receptors present on almost all cells. <sup>[5,6]</sup>

Vit D deficiency/insufficiency has been implicated in increasing the incidence and severity of various immuno-inflammatory diseases like psoriasis, atopic dermatitis etc. Various authors have found correlation between presence of type 1 hypersensitivity diseases like asthma, atopic dermatitis, rhinosinusitis, food allergy and Vit D deficiency as it is known to extensively

influence proliferation, survival, differentiation, and function of mast cells.<sup>[7,8]</sup> Few studies have also suggested that Vit D inhibits development of allergic diseases and can be a potential treatment for allergy.<sup>[9]</sup> Various studies have shown beneficial effect of vitamin D supplementation in urticaria disease in other populations.<sup>[10-12]</sup> However the role of Vit D in urticaria is inconclusive in our population with whatever limited studies are available in literature. Thus we wanted to see the effect of serum Vit D supplementation in course of CSU in our urticaria patients.

## **Review of literature**

In a study done by Rorie A et al in 2014<sup>[13]</sup> they reported significant decrease (40%) in total urticaria severity scores (USS) in the high, but not low, vitamin D3 treatment group by week 12. Compared with low treatment, the high treatment group demonstrated a trend ( $P < .052$ ) toward lower total USS scores at week 12, which was driven by significant decreases in body distribution and number of days with hives. Beneficial trends for sleep quality and pruritus scores were observed with high vitamin D3. Serum 25-hydroxyvitamin D levels increased with high vitamin D3 supplementation, but there was no correlation between 25-hydroxyvitamin D levels and USS scores.

In another study by Topal IO et al<sup>[14]</sup> they reported serum 25(OH)D concentration was significantly lower in CSU group compared to healthy subjects ( $p < 0.001$ ). The prevalence of vitamin D deficiency ( $< 20$  (mg/L) and insufficiency ( $< 30$  mg/L) was significantly higher in CSU patients than control groups. In addition, 25(OH)D concentrations were significantly lower in

both mild-moderate and severe CSU patients than those of the controls ( $p < 0.011$  and  $p = 0.001$ , respectively). Ninety eight percent of patients ( $25(\text{OH})\text{D} < 30 \text{ ng/L}$ ) were treated with vitamin D3 (300 000 IU/month) supplementation, and after 12 weeks, these patients showed significant improvements in UAS4 and CU-Q2oL scores. Conclusion: This study support the contributing and beneficial effects of vitamin D in the treatment of CU. Replacement of vitamin D may provide improvement in both the severity of symptoms and the quality of life scores in these patients

In another recent study by Rasool R et al in 2015, <sup>[15]</sup>they evaluated role of Vitamin D supplementation in urticaria patients and reported low serum levels of  $25(\text{OH})\text{D}$  was observed in 91% of CU patients and 64% of the healthy controls ( $P < 0.0001$ ). Visual analogue score (VAS) and 5-D itch Score in subgroups Vitamin D, antihistamines and VD + antihistamines + steroids decreased significantly from  $6.7 \pm 0.043$ ,  $6.6 \pm 0.42$  and  $6.68 \pm 0.40$  at baseline to  $5.2 \pm 0.70$  ( $P = 0.0088$ ),  $3.3 \pm 0.50$  ( $P < 0.0001$ ) and  $1.86 \pm 0.39$  ( $P < 0.0001$ ) after treatment and from  $14.5 \pm 0.72$ ,  $13.9 \pm 0.77$  and  $13.9 \pm 0.221$  to  $12.06 \pm 1.10$  ( $P = 0.0072$ ),  $8.1 \pm 1.13$  ( $P < 0.0001$ ) and  $5.01 \pm 0.94$  ( $P < 0.0001$ ) respectively.

## **METHODOLOGY**

### **Aims and Objectives**

Aim of the study the role of vitamin D supplementation in patients with chronic urticaria

### **Primary Objectives'**

1. To study Vitamin D deficiency in patients with Chronic urticaria as compared to controls
2. To compare factors associated with vitamin D deficiency in patients of chronic urticaria

### **Secondary objective**

To study the effect of vitamin D supplementation in patients of chronic Urticaria

### **Materials and methods**

**Sample size:** Three hundred patients with chronic urticaria and 300 healthy controls

Sampling method: Convenient sampling

### **Study population:**

Study populations consisted of CSU patients and age and sex matched healthy controls having same Fitzpatrick skin type IV and V

### **Inclusion criteria**

Adults (>18 years) having history of urticaria at least 2 days per week for 6 weeks or longer with/without angioedema and healthy adult controls.

### **Exclusion criteria**

1. Patients with pure physical urticaria, only dermatographism, urticarial vasculitis, hereditary or acquired angioedema
2. Patients with BMI>25 kg/m<sup>2</sup>, dyslipidemia, diabetes, hypertension, pre-existing cardiovascular disease, cerebro-vascular accidents, smokers, and other systemic or cutaneous disorders including atopic dermatitis, psoriasis etc
3. Patients with hypercalcemia (>11 mg/dL), renal insufficiency, hepatic disorders, hyperparathyroidism, sarcoidosis, other granulomatous disorders, malignancy.

Recruitment of cases and controls to be done simultaneously in summer over a period of 3 months.

### **Clinical and laboratory analysis**

Each patient will undergo investigations including: routine laboratory tests (full blood count, urine analysis, serum glucose, hepatic functions, and creatinine, ESR, eosinophil, and total IgE), antinuclear and antithyroid microsomal antibodies, thyroid function tests, chest X-ray and abdominal ultrasonography. Additionally, dental, and ENT consultations as well as the autologous serum skin test (ASST) and autologous plasma skin test (APST) [10].

### **Data Collection**

Blood will be collected at enrollment and at 0, 6- and 12-week clinic visits and processed at the institution's clinical laboratory for serum Vit D, calcium, albumin, phosphorus, creatinine, serum urea nitrogen, inorganic phosphorus, and intact parathyroid hormone for study and safety end points. Spot urine for urine calcium will also be collected for safety end points. Serum Vit D concentration will be measured with the use of an automated direct Electrochemiluminescence immunoassay (Elecsys, Roche Diagnostic, Mannheim, Germany). To assess the Vit D status, the subjects will be divided into four groups according to serum Vit D levels: deficient ( $<10$  ng/ml), very low (10-19 ng/ml), insufficiency (between 20 and 29 ng/ml), and sufficiency/normal ( $\geq 30$  ng/ml)<sup>17</sup>

### **Assessing severity**

The urticaria activity score over 4 days (UAS4) will be used to assess the disease severity using number of wheals and pruritus intensity based on the EAACI/GA2LEN/EDF guidelines.<sup>[16]</sup> The

patient's disease severity levels to be graded as mild (0-8), moderate (9-16), and severe (17-24). [17].

## **Study Design**

This is a prospective, randomized, single center clinical study. Serum Vit D level will be assessed in all patients at baseline. Patient with Vit D level  $\geq 30$  will be excluded from the trial but included in the study and those with Vit D level  $< 30$  will be randomized into 3 groups A, B and C. The randomization method is to be done using randomized blocks with block sizes of 3 and 6 to ensure a balance in treatment assignment over time. The randomization list is to be generated by computer generated table. Patients with Vit D level  $\geq 30$  will be categorized into Group D. Patients belonging to Group A will be treated with low dose Vit D (2000 IU/day) according to Indian council of medical research (ICMR) guidelines. Those in Group B will be treated with high dose Vit D (60,000 IU/week) and group C will not be given any Vit D supplements. Patients belonging to Group A and B will be treated for 12 weeks in order to safely restore Vit D and achieve a steady state. In addition levocetirizine 10 mg will be given to all patients in groups to control urticaria symptoms. All patients were treated according to EAACI/GA2LEN/EDF guidelines<sup>[16]</sup>. Subjects will also be provided with rescue prednisone use for intolerable or uncontrolled symptoms. At 6 weeks and 12 weeks, a physician assessment (physician blinded to treatment arm) will be conducted to check if patients had intolerable symptoms or took rescue prednisolone 40 mg therapy. Safety monitoring will be completed throughout the entirety of the study. Specific stopping rules and discontinuation of the study include pregnancy, a serum Vit D level higher than 100 ng/mL, or a serum calcium level higher than 11 mg/dL. Patients will be followed for 2 weeks after the study completion and thereafter data analysis will be done in 3 steps:

Step 1: Comparison of serum Vit D level in CSU patients vs. controls

Step 2: Assessment of factors associated with Vit D deficiency in urticaria patients

Step 3: Effect of Vit D supplementation (group A (low dose), group B (high dose), group C(no supplementation) on urticaria severity using UAS4

### **Statistical analysis:**

The statistical analyses will be performed with the help of SPSS statistical software, version 20.0, IBM SPSS, version 20 (SPSS, Inc., Chicago IL, USA),  $P < 0.05$  as significant. For normally distributed data means will be compared using unpaired t-test for two groups. For skewed data Mann-Whitney test will be applied. For categorical variables number and percentages will be calculated. Chi-sq test or Fisher's exact test will be applied for categorical data. Comparison of serum Vit D level in CSU patients vs. controls will be performed using t-test. Assessment of factors associated with Vit D deficiency in urticaria patients will be performed using multivariate regression analysis and effect of Vit D supplementation (group A (low dose), group B (high dose), group C(no supplementation) on urticaria severity using UAS4 will be assessed using ANOVA.

### **Primary Outcome**

1. To compare the Vitamin D deficiency in chronic urticaria patients vs controls
2. To compare the effect of vitamin D supplementation in patients of chronic urticaria

### **Ethical justification:**



This is randomized controlled prospective study to evaluate the role of Vitamin D in chronic urticaria. In this study we are treating only patients with low vitamin D (<30ng/ml) with Vitamin D supplementation and studying its effect on urticaria severity. Patients with normal vitamin D (>30ng/ml) are not treated. Also no patient is denied treatment as all patients are treated with antihistaminics. No additional treatment is given to patients. Urticaria treatment is done in accordance with EACCI/GA2LEN international guidelines. [16] Regular Vitamin D, PTH, S. Calcium and phosphate analysis is done to avoid any risk of hypervitaminosis.. All the investigations mentioned are routinely done in urticaria clinic as per EACCI/GA2LEN [16] international urticaria guidelines. This study will help us if vitamin D supplementation will help in better control of urticaria symptoms. All the investigations mentioned are routinely done in urticaria clinic as per EACCI/GA2LEN international urticaria guidelines

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## Case record form

**Name:**

**CR No:**

**Age/Sex:**

Address:

Phone No:

### Chief Complains

#### History:

Age of onset:

Symptoms:-

Angioedema (Yes/NO)

Family history of Atopy-(Yes/NO)

Thyroid abnormalities- – Present/Absent

Family history of similar disease- (Yes/NO) If yes then in whom

Any other systemic illness-

H/o any drug intake– Present/ Absent

Duration of Sun exposure per day- (<30 min, 30min-1 hour, 1-1.5 hours, 1.5-2 hours, >2 hours)

-

#### General Physical Examination

Height-

Weight

BMI-

Pulse:

BP:

RR-

Temp-

Baseline UAS-

Clinical signs suggestive of Atopy:

#### Investigation (with date)

full blood count

urine analysis

serum glucose

LFT

RFT

ESR

total IgE

S.Vit D level-

S.PTH-

S.Ca-

S.PO4-

ANA

antithyroid microsomal antibodies

Thyroid function tests

chest X-ray

Autologous serum skin test (ASST) and autologous plasma skin test (APST)

Urine routine and microscopy:

Investigations	0 weeks	6 weeks	12 weeks	18 weeks
Vit D				
S. calcium				
S. phosphorus,				
intact parathyroid hormone				
Spot urine for calcium				

**Treatment given**

**Next Follow up**

**UAS at 6 weeks**

**UAS at 12 weeks**

**UAS at 18 weeks**

## IEC Assent Form

PROTOCOL NO:

SPONSOR:

PRINCIPAL INVESTIGATOR: Dr. M.Sendhil Kumaran

Name of Participant:

Title: - **A randomized controlled trial to evaluate the effect of Vitamin D supplementation in patients with Chronic Urticaria**

We are doing a research study. I am your doctor and principal investigator –Dr.M. Sendhil Kumaran

We are doing this study to find out the effect of Vitamin D supplementation on chronic urticaria which will allow us to control the disease more effectively

We are asking you to take part in this study because you it is a common disease and it will help us in treating Vitamin D deficiency in you as well. But we will only take you if you allow us. If you do not want to do so your treatment will continue as usual. If you decide to take part now but wish to discontinue later, you can tell us and we will take you out of the study.

Once you agree to take part, you will have to undergo Blood sample for biochemistry (S. Vit D, PTH, Ca, PO<sub>4</sub>,ALP), Urine sample (Urine Ca, creatinine) The clinical examination, investigations to be done are safe and standard. They are routinely done in urticaria clinic as part of our treatment protocol

It is possible that the study will help you feel better. It can also occur that you do not get any benefit but the information we get from you may help other children in future.

We have asked your parents [or guardian] their permission and it is all right with them. Do not hesitate to ask questions. You can also ask us about anything later on if there are no questions right now.

### Assent form

	Child's signature
I have been explained about the study and I agree to take part in it.	

Child's Name:

Date:

Certificate by the Investigator (his/her representative obtaining assent) :

Tick one    Signature of the  
Investigator /  
representative

The child can read the assent form and was able to understand it

The child was not capable of reading the assent form, but I verbally explained the information.

Name of Investigator / representative:

Date:

## **Participant Information Sheet (PIS)**

PROTOCOL NO:

SPONSOR:

PRINCIPAL INVESTIGATOR: Dr. M.Sendhil Kumaran

Name of Participant:

Title:

1. You are invited to take part in this research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

2. **What is your expected duration of the participation?**

Your participation in this study will last for a total of 18 weeks

3. **What procedures will be followed during this study?**

You will have to undergo Blood sample for biochemistry (S. Vit D, PTH, Ca, PO<sub>4</sub>, ALP, VIT D polymorphism), Urine sample (Urine Ca, creatinine)

4. **What are the risks and discomforts to you?**

The clinical examination, investigations to be done are safe and standard. Taking blood sample for biochemical analysis may cause slight pain but is routinely done as part of urticaria management

5. **What benefits are expected from this research?**

This study will help us in Vitamin D deficiency in patients of chronic urticaria and factors associated with it. It will also help in finding out if vitamin D supplementation improves urticaria control in patients.

6. **What are the alternatives available to you?**

You will only be given vitamin D supplementation if your vitamin D level is low (<30ng/ml) and rest care will be the same as other patients. Antihistamines will be given to you for the urticaria disease control

7. **Are the data/records of the participant kept confidential?**

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, institutional ethics committee to view your data, if required.

8. **What will be the treatment schedule(s)?**

If you participate in the study you will be given Vitamin D supplementation in addition to levocetirizine for 12 weeks. Thereafter supplementation will be stopped and only



antihistaminics will be continued for the disease control

9. **What compensation and/or treatment(s) are available to the Participant in the event of a trial-related injury?**

No compensation will be awarded however in the eventuality of any trial related injury (which is unlikely) you will be given treatment at PGIMER at no additional costs.

10. **Whom to contact for trial related queries and what are the rights of Participants in the event of any injury?**

You can contact the Principal investigator (Dr M. Sendhil Kumaran) in the event of any injury.

11. **Are the participants paid to take part in this study?**

No payments will be given for participation in the study

12. **What are your responsibilities during participation in the study?**

You will be required to come for the investigations and follow up as per treatment schedule. You will be called for 6 weekly follow up till completion of trial (18 weeks) and thereafter as per your regular clinic scheduled visits

13. Participation is voluntary, that the Participant can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Participant is otherwise entitled.

14. Participant or Participant's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Participant's willingness to continue participation will be provided.

15. If the participant is unable to come for follow up then his/her participation may be terminated by the Investigator without the Participant's consent.

16. There will be no additional costs to the Participant that may result from participation in the study.

17. Approximate number of Participants enrolled in the study- 300

18. Any other pertinent information- No

**Contact persons:**

For further information / questions, you can contact us at the following address:

Principal Investigator:

Dr. M. Sendhil Kumaran  
Associate Professor

Dept. of Dermatology, Venereology & Leprology  
Tel:

**Co-Investigator**

Prof. Dr. Davinder Prasad

Head of Department, Dept. of Dermatology, Venereology & Leprology

Contact person(s):

Dr. M.Sendhil Kumaran

Associate Professor

Dept. of Dermatology, Venereology & Leprology

Email: drsen\_2000@yahoo.co.in

Tel: 8872004023

In case of conflicts, you can contact the chairperson (convener) of our institutional ethics committee at the following address:

Convener/Chairperson, Institutional Ethics Committee

PGIMER, Chandigarh

Telephone: .....

## Informed Consent Form (ICF)

**Study Title: A randomized controlled trial to evaluate the effect of Vitamin D supplementation in patients with Chronic Urticaria**

Study Number (if any): \_\_\_\_\_

Subject's Initials: \_\_\_\_\_

Subject's Name: \_\_\_\_\_

Date of Birth / Age: \_\_\_\_\_

	Participant's initial
1. I confirm that I have read and understood the information sheet dated _ _ _ _ for the above study and have had the opportunity to ask questions.	
2. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
3. I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.	
4. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)	
5. I agree to take part in the above study	

Signature (or Thumb impression) of the Subject/Legally Acceptable

Representative: \_\_\_\_\_

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Signatory's Name: \_\_\_\_\_

Signature of the Investigator: \_\_\_\_\_ Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Study Investigator's Name: \_\_\_\_\_

1. No such/similar study has been conducted in the department
2. Role of Vitamin D in chronic urticaria has been proven in case series and few studies. However randomized controlled trials are lacking. Hence Serum vitamin D level assessment and supplementation is routinely done in urticaria clinic of our department of Dermatology but as far as assessing the improvement in severity of urticarial post Vitamin D supplementation hasn't been noted by us. This study will help us in formulating Vitamin D supplementation protocol in urticaria clinic patients.
3. Vitamin D supplementation will be done in all control patients also after 12 weeks, once the study period gets over, because they are in turn chronic urticarial patients.
4. Sample size calculation, assuming  $\alpha=0.05$  and power  $(1-\beta)= 0.8$  and  $p_1 =$  expected proportion of the outcome in group 1= 0.7 and  $p_2 =$  expected proportion of the outcome in group 2= 0.8, based on previous studies quoted in the protocol and on adjustment for size for attrition rate, the sample size ( $N$ ) has to be multiplied by the correction factor  $100/100-X$ , where  $X =$  dropout rate in percentage (%).Lehr's formula is a quick calculation of sample size for power of 80% and a two-tailed significance level of 0.05. The required size of each of two equal groups is  $16/\delta^2$ . Estimated sample size is 136 and with 10% drop out rate it is 149 so we have included 150 patients in both groups

5. Since vitamin D assessment is done for all urticaria patients in clinic this will be a routine evaluation for them. In addition we plan to submit it for grant approval once ethics committee approval is given
6. Yes, all the investigations done are routinely done at the same frequency as proposed in the study based on previous studies which have been quoted in the protocol. All patients with deficient level will be treated, controls will also be treated after 12 weeks once gets period is over
7. Separate information sheet for controls attached with this form. Controls will be from department of dermatology with diseases other than urticaria.
8. Ethical justification: This is randomized controlled prospective study to evaluate the role of Vitamin D in chronic urticaria. In this study we are treating patients with low vitamin D ( $<30\text{ng/ml}$ ) with Vitamin D supplementation and studying its effect on urticaria severity. Patients with normal vitamin D ( $>30\text{ng/ml}$ ) are not treated. Also no patient is denied treatment as all patients are treated with antihistaminics to control urticaria symptoms. This study will help us if vitamin D supplementation will help in better control of urticaria symptoms. Urticaria treatment is done in accordance with EACCI/GA2LEN international guidelines. Regular monitoring of Vitamin D, PTH, S. Calcium and phosphate analysis is done to avoid any risk of hypervitaminosis. All the investigations mentioned are routinely done in urticaria clinic as per EACCI/GA2LEN international urticaria guidelines.

9. Information sheet attached in all details
10. All investigators are from urticaria clinic as they will be able to assess the disease control and urticaria activity once patients come for follow up.

## **Participant Information Sheet (PIS) for Urticaria patients**

PROTOCOL NO:

SPONSOR:

PRINCIPAL INVESTIGATOR: Dr. M.Sendhil Kumaran

Name of Participant:

Title:

19. You are invited to take part in this research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.

**20. What is your expected duration of the participation?**

Your participation in this study will last for a total of 18 weeks.

**21. What procedures will be followed during this study?**

You will have to undergo Blood sample for biochemistry (S. Vit D, PTH, Ca, PO<sub>4</sub>, ALP), Urine sample (Urine Ca, creatinine) at 0, 6 and 12 weeks. After S. Vitamin D assessment at 0 weeks, patients with Serum Vit D level <30 ng/ml will be divided into three groups A, B and C and treated with high dose (60,000IU/week), low dose (2000 IU/day) and no supplementation for 12 weeks. This will be done randomly without any bias. Once patient is allotted to one particular group he will be treated according to the protocol of that group as described above and above mentioned investigations will be done at 0, 6 and 12 weeks. After 12 weeks all patients with vitamin D level <30 ng/ml will be treated with 60,000IU/week till level becomes normal.

**22. What are the risks and discomforts to you?**

The clinical examination, investigations to be done are safe and standard. Taking blood sample for biochemical analysis may cause slight pain but is routinely done as part of urticaria management

**23. What benefits are expected from this research?**

This study will help us in Vitamin D deficiency in patients of chronic urticaria and factors associated with it. It will also help in finding out if vitamin D supplementation improves urticaria control in patients.

**24. What are the alternatives available to you?**

You will only be given vitamin D supplementation if your vitamin D level is low (<30ng/ml) and rest care will be the same as other patients. Antihistamines will be given to you for the urticaria disease control

**25. Are the data/records of the participant kept confidential?**

You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history).

By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, institutional ethics committee to view your data, if required.

**26. What will be the treatment schedule(s)?**

If you participate in the study you will be given Vitmain D supplementation in addition to levocetirizine for 12 weeks. Thereafter supplementation will be stopped and only antihistaminics will be continued for the disease control.

**27. What compensation and/or treatment(s) are available to the Participant in the event of a trial-related injury?**

No compensation will be awarded however in the eventuality of any trial related injury (which is unlikely) you will be given treatment at PGIMER at no additional costs.

**28. Whom to contact for trial related queries and what are the rights of Participants in the event of any injury?**

You can contact the Prinicipal investigator(Dr M.Sendhil Kumaran) in the event of any injury.

**29. Are the participants paid to take part in this study?**

No payments will be given for participation in the study

**30. What are your responsibilities during participation in the study?**

You will be required to come for the investigations and follow up as per treatment schedule. You will be called for 6 weekly follow up till completion of trial (18 weeks) and thereafter as per your regular clinic scheduled visits

31. Participation is voluntary, that the Participant can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Participant is otherwise entitled.

32. Participant or Participant's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Participant's willingness to continue participation will be provided.

33. If the participant is unable to come for follow up then his/her participation may be terminated by the Investigator without the Participant's consent.

34. There will be no additional costs to the Participant that may result from participation in the study.

35. Approximate number of Participants enrolled in the study- 150

36. Any other pertinent information- No



**Contact persons:**

For further information / questions, you can contact us at the following address:

**Principal Investigator:**

Dr. M. Sendhil Kumaran  
Associate Professor  
Dept. of Dermatology, Venereology & Leprology  
Tel:

**Co-Investigator**

Prof. Dr. Davinder Prasad  
Head of Department, Dept. of Dermatology, Venereology & Leprology

**Contact person(s):**

Dr. M. Sendhil Kumaran  
Associate Professor  
Dept. of Dermatology, Venereology & Leprology  
Email: drsen\_2000@yahoo.co.in  
Tel: 8872004023

In case of conflicts, you can contact the chairperson (convener) of our institutional ethics committee at the following address:

Convener/Chairperson, Institutional Ethics Committee  
PGIMER, Chandigarh  
Telephone: .....

## Participant Information Sheet (PIS) for controls

PROTOCOL NO:

SPONSOR:

PRINCIPAL INVESTIGATOR: Dr. M.Sendhil Kumaran

Name of Participant:

Title:

1. You are invited to take part in this research study. The information in this document is meant to help you decide whether or not to take part. Please feel free to ask if you have any queries or concerns.
2. **What is your expected duration of the participation?**  
Your participation in this study will last for a total of 18 weeks
3. **What procedures will be followed during this study?**  
You will have to undergo Blood sample for biochemistry (S. Vit D, PTH, Ca, PO<sub>4</sub>,ALP) at baseline
4. **What are the risks and discomforts to you?**  
The clinical examination, investigations to be done are safe and standard. Taking blood sample for biochemical analysis may cause slight pain but is routinely done
5. **What benefits are expected from this research?**  
This study will help us in Vitamin D deficiency in patients of chronic urticaria and factors associated with it. It will also help in finding out if vitamin D supplementation improves urticaria control in patients. It will also help in assessing if vitamin D deficiency is more prevalent in urticaria patients over normal controls
6. **What are the alternatives available to you?**  
You will only be given vitamin D supplementation if your vitamin D level is low (<30ng/ml) and rest care will be the same as other patients. Antihistamines will be given to you for the urticaria disease control
7. **Are the data/records of the participant kept confidential?**  
You have the right to confidentiality regarding the privacy of your medical information (personal details, results of physical examinations, investigations, and your medical history). By signing this document, you will be allowing the research team investigators, other study personnel, sponsors, institutional ethics committee to view your data, if required.
8. **What will be the treatment schedule(s)?**  
If you participate in the study you will be given Vitamin D supplementation in addition to treatment for your primary disease if found deficient .
9. **What compensation and/or treatment(s) are available to the Participant in the event of a trial-related injury?**  
No compensation will be awarded however in the eventuality of any trial related injury (which is unlikely) you will be given treatment at PGIMER at no additional costs.

10. **Whom to contact for trial related queries and what are the rights of Participants in the event of any injury?**

You can contact the Principal investigator(Dr M.Sendhil Kumaran) in the event of any injury.

11. **Are the participants paid to take part in this study?**

No payments will be given for participation in the study

12. **What are your responsibilities during participation in the study?**

You will be required to come for the investigations and follow up as per your disease treatment schedule. No additional follow ups visits.

13. Participation is voluntary, that the Participant can withdraw from the study at any time and that refusal to participate will not involve any penalty or loss of benefits to which the Participant is otherwise entitled.

14. Participant or Participant's representative will be notified in a timely manner if significant new findings develop during the course of the research which may affect the Participant's willingness to continue participation will be provided.

15. If the participant is unable to come for follow up then his/her participation may be terminated by the Investigator without the Participant's consent.

16. There will be no additional costs to the Participant that may result from participation in the study.

17. Approximate number of Participants enrolled in the study- 150

18. Any other pertinent information- No

**Contact persons:**

For further information / questions, you can contact us at the following address:

**Principal Investigator:**

Dr. M. Sendhil Kumaran  
Associate Professor  
Dept. of Dermatology, Venereology & Leprology  
Tel:

**Co-Investigator**

Prof. Dr. Davinder Prasad  
Head of Department, Dept. of Dermatology, Venereology & Leprology

**Contact person(s):**

Dr. M.Sendhil Kumaran

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Email: drsen\_2000@yahoo.co.in  
Tel: 8872004023

In case of conflicts, you can contact the chairperson (convener) of our institutional ethics committee at the following address:

Convener/Chairperson, Institutional Ethics Committee  
PGIMER, Chandigarh  
Telephone: .....

## Informed Consent Form (ICF) for cases and controls

Study Title: **A randomized controlled trial to evaluate the effect of Vitamin D supplementation in patients with Chronic Urticaria**

Study Number (if any): \_\_\_\_\_

Subject's Initials: \_\_\_\_\_

Subject's Name: \_\_\_\_\_

Date of Birth / Age: \_\_\_\_\_

	Participant's initial
6. I confirm that I have read and understood the information sheet dated _ _ _ _ for the above study and have had the opportunity to ask questions.	
7. I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	
8. I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.	
9. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s)	
10. I agree to take part in the above study	

Signature (or Thumb impression) of the Subject/Legally Acceptable

Representative: \_\_\_\_\_

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Signatory's Name: \_\_\_\_\_

Signature of the Investigator: \_\_\_\_\_

Date: \_\_\_\_/\_\_\_\_/\_\_\_\_

Study Investigator's Name: \_\_\_\_\_

